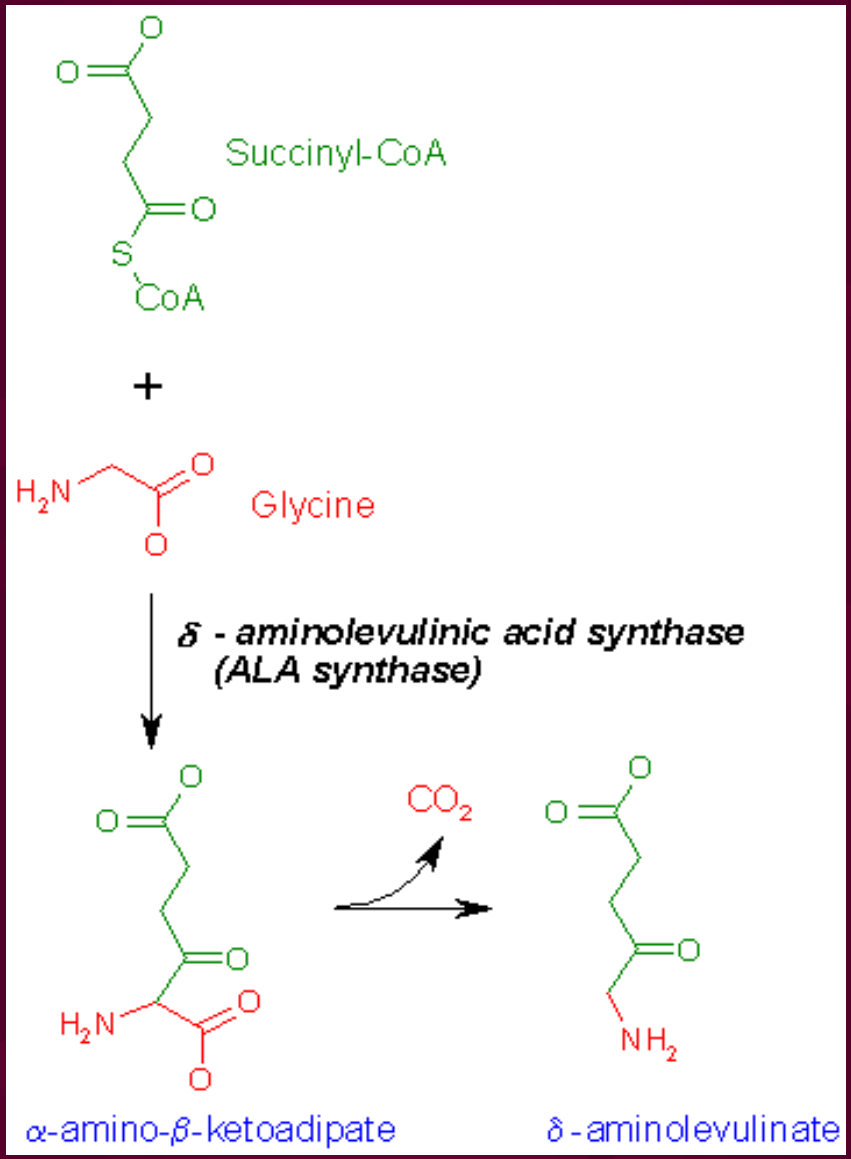
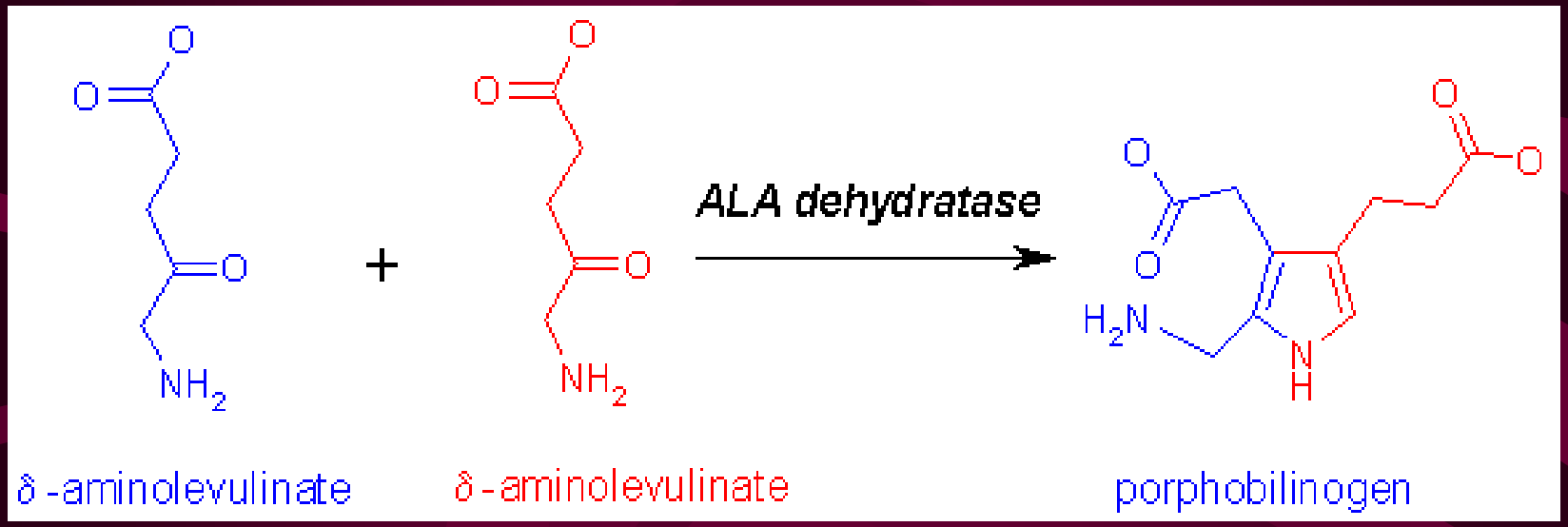
Porphyrines

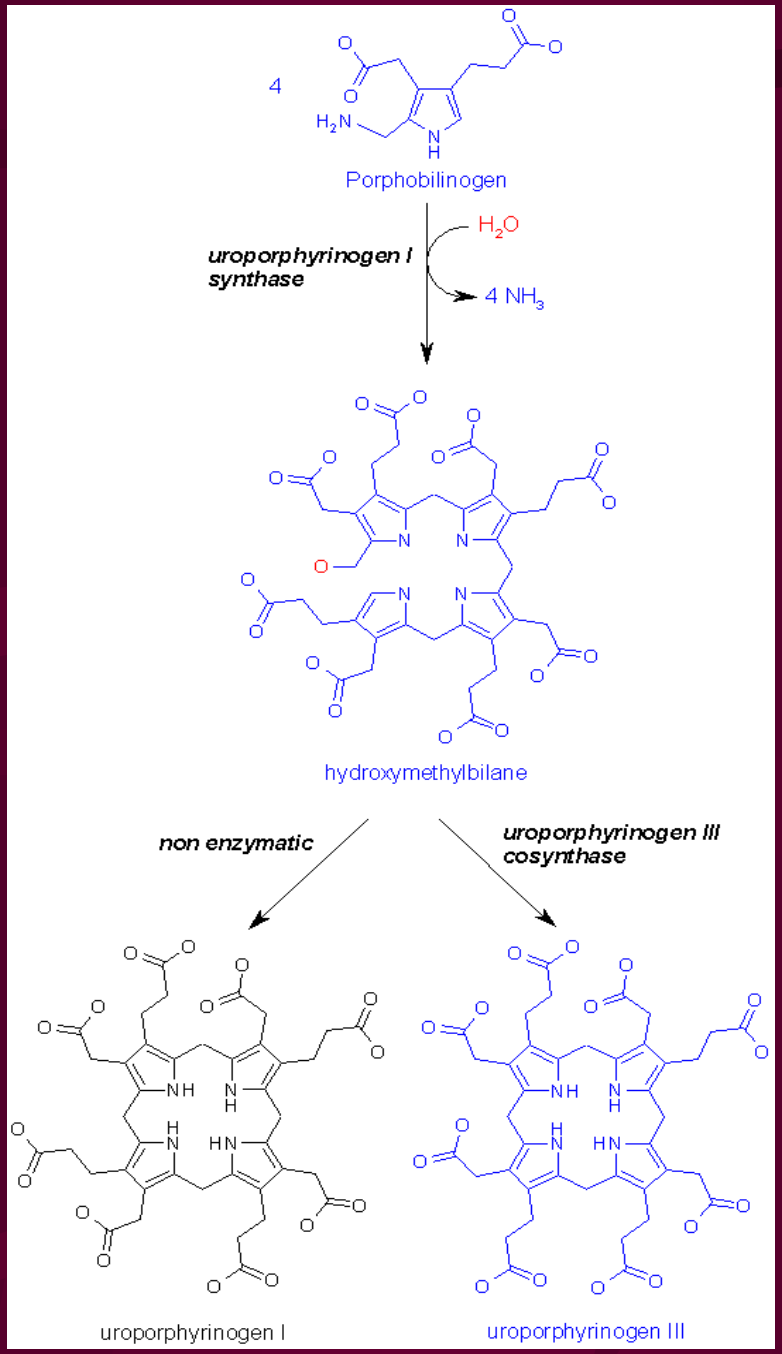
Overview of Porphyrias

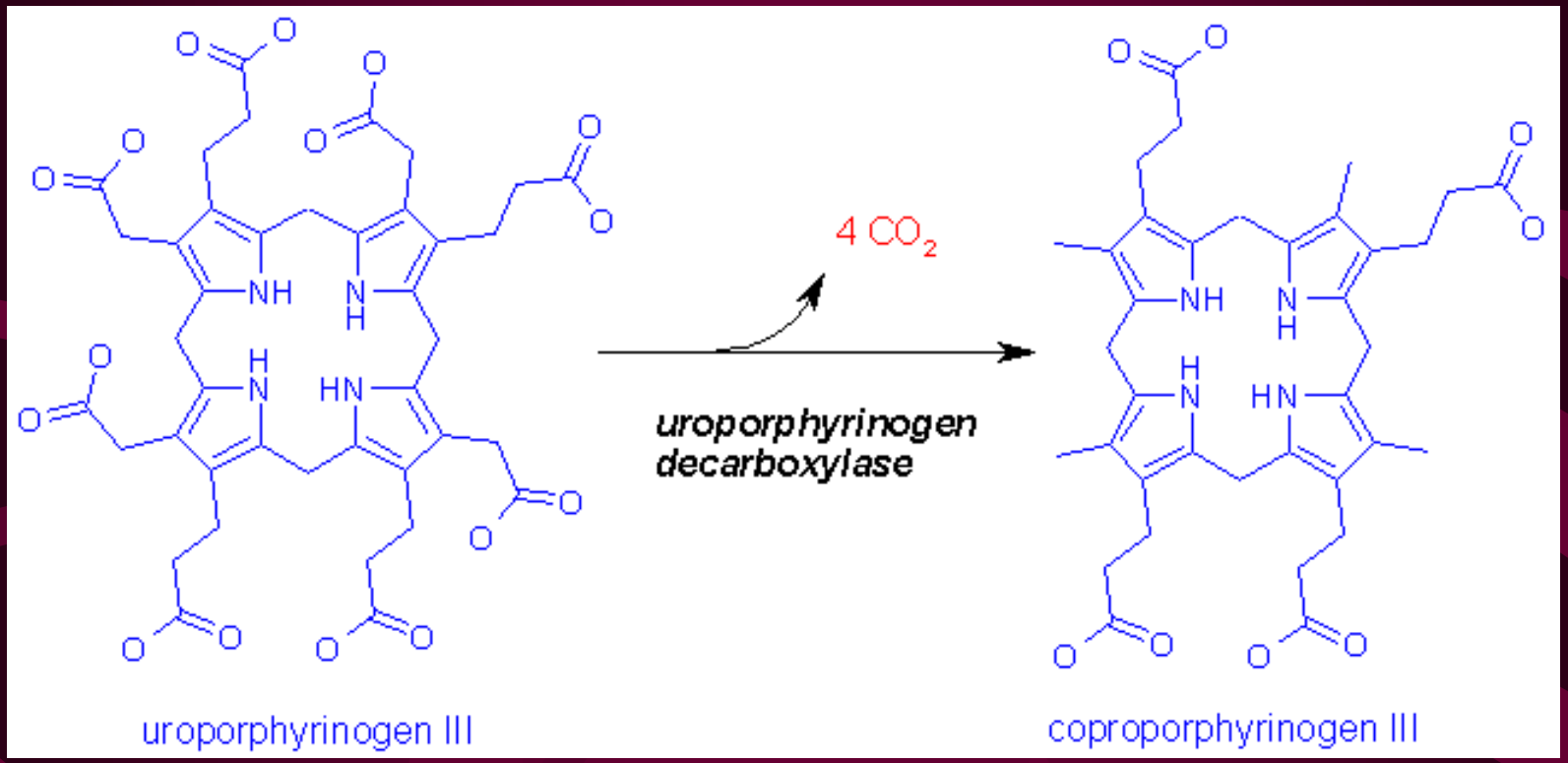
- Metabolic disorders involving defects in heme biosynthesis
- May be inherited or acquired
- Most inherited forms are autosomal dominant, some are autosomal recessive

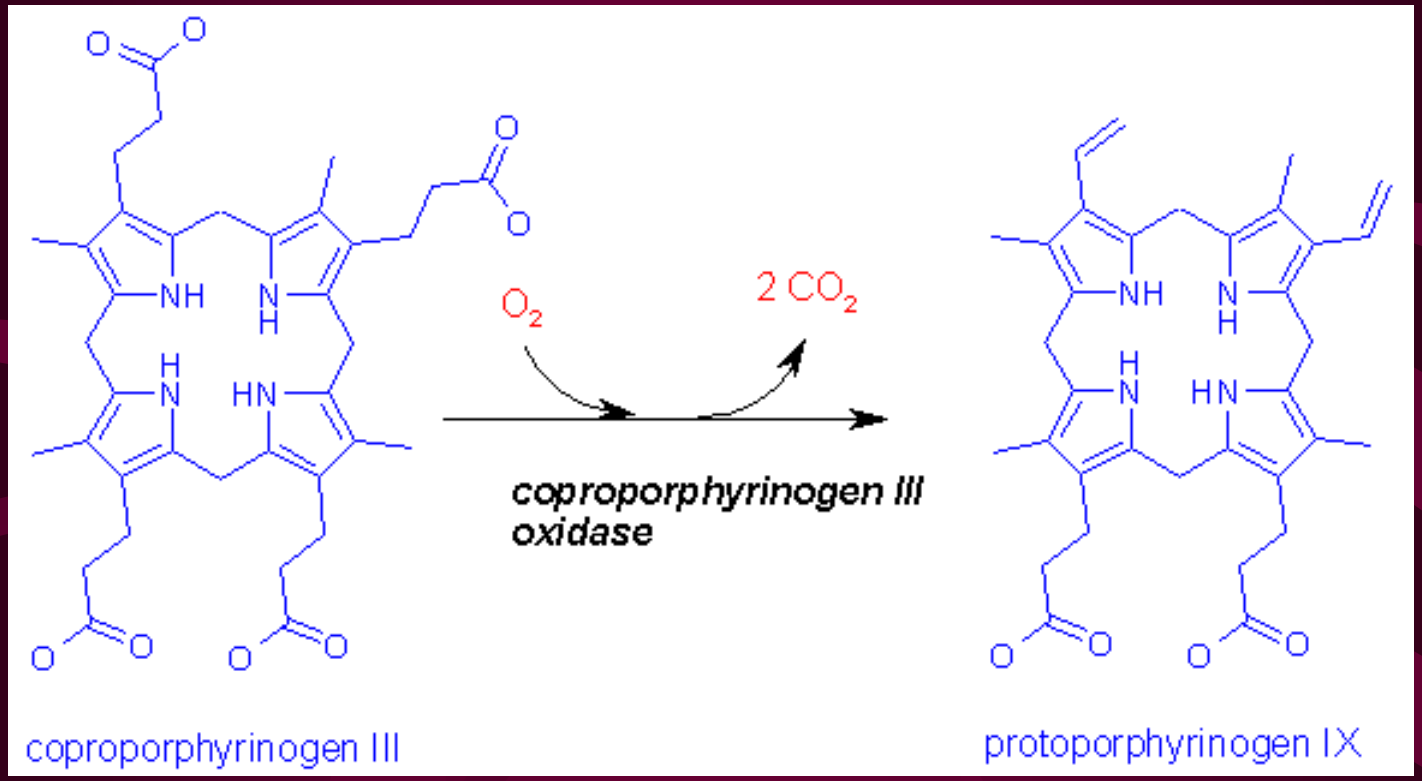
Heme Biosynthesis




O
O
O
NH2
+
O
O
O
NH2
ALA dehydratase
O
O
O
H2N
N
H
O
δ-aminolevulinate
δ-aminolevulinate
porphobilinogen

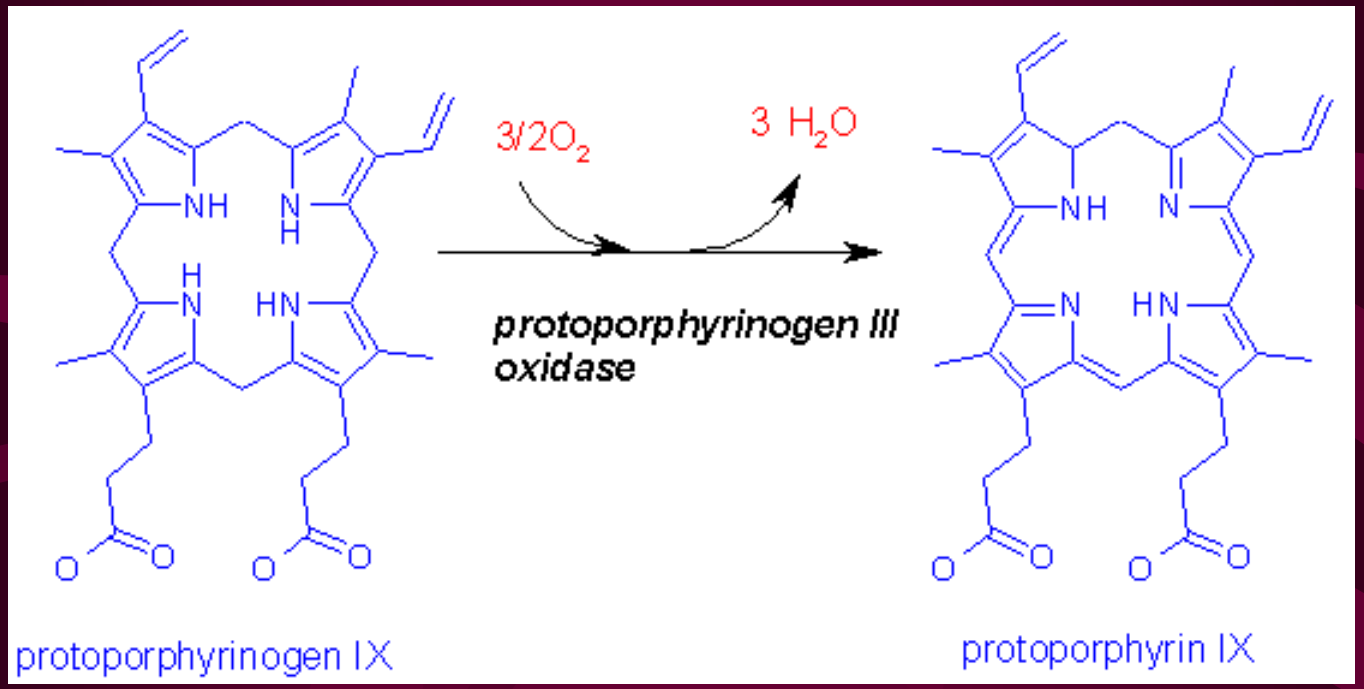

4
Porphobilinogen
uroporphyrinogen I synthase
H_2O
4 NH_3
hydroxymethylbilane
non enzymatic
uroporphyrinogen III cosynthase
uroporphyrinogen I
uroporphyrinogen III

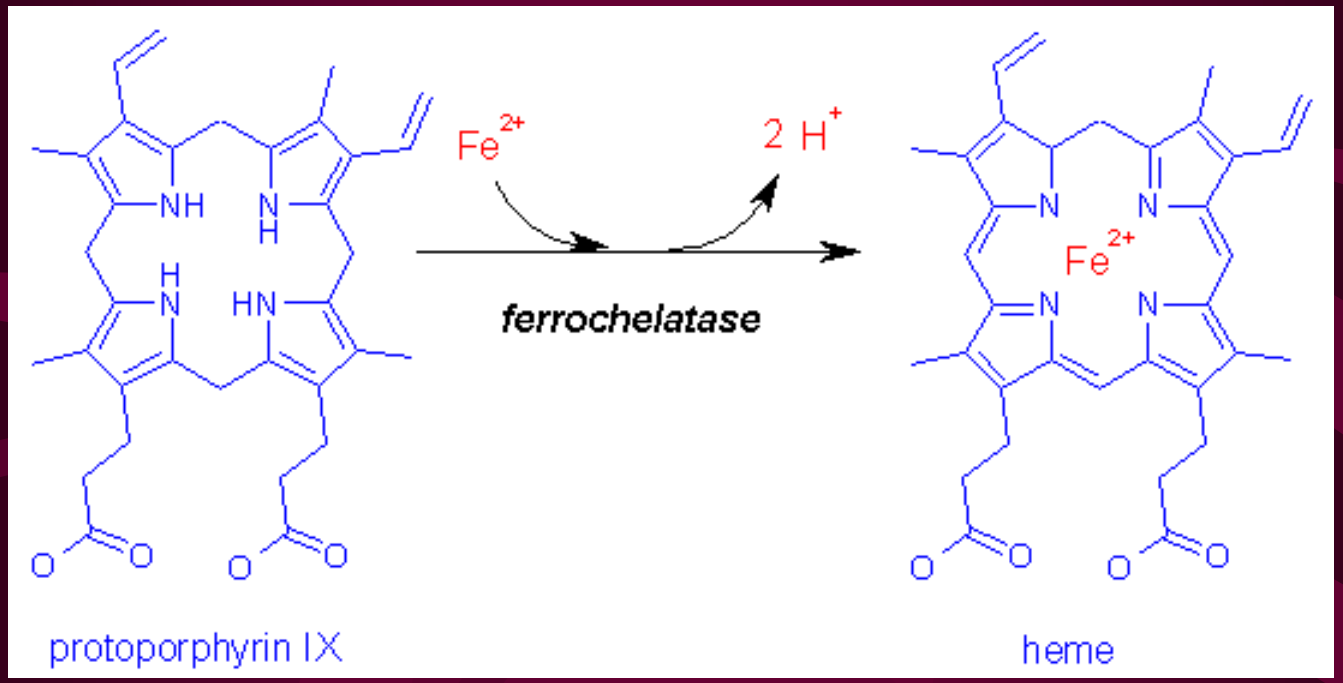

4 CO2
uroporphyrinogen
decarboxylase
uroporphyrinogen III
coproporphyrinogen III

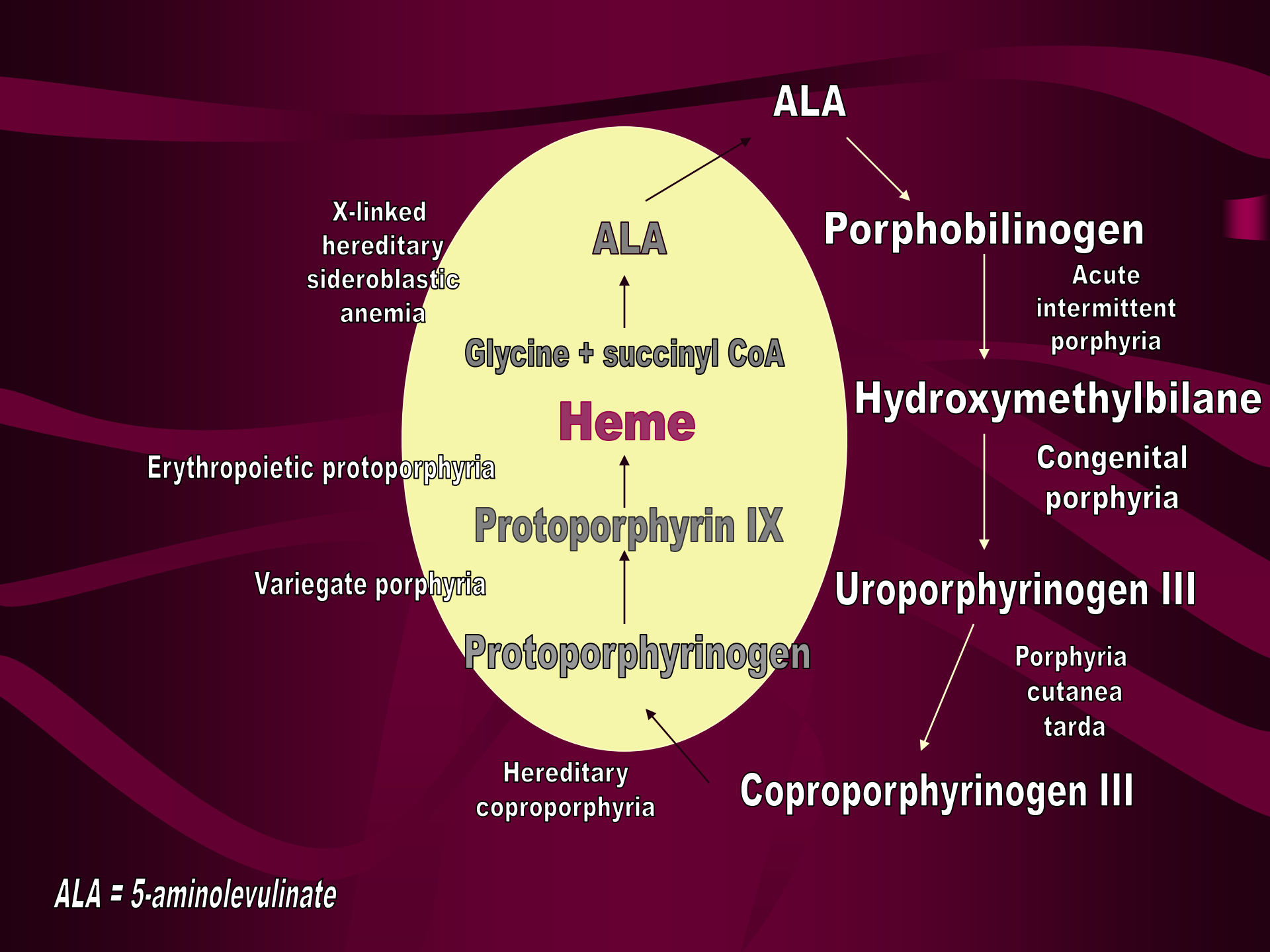


coproporphyrinogen III

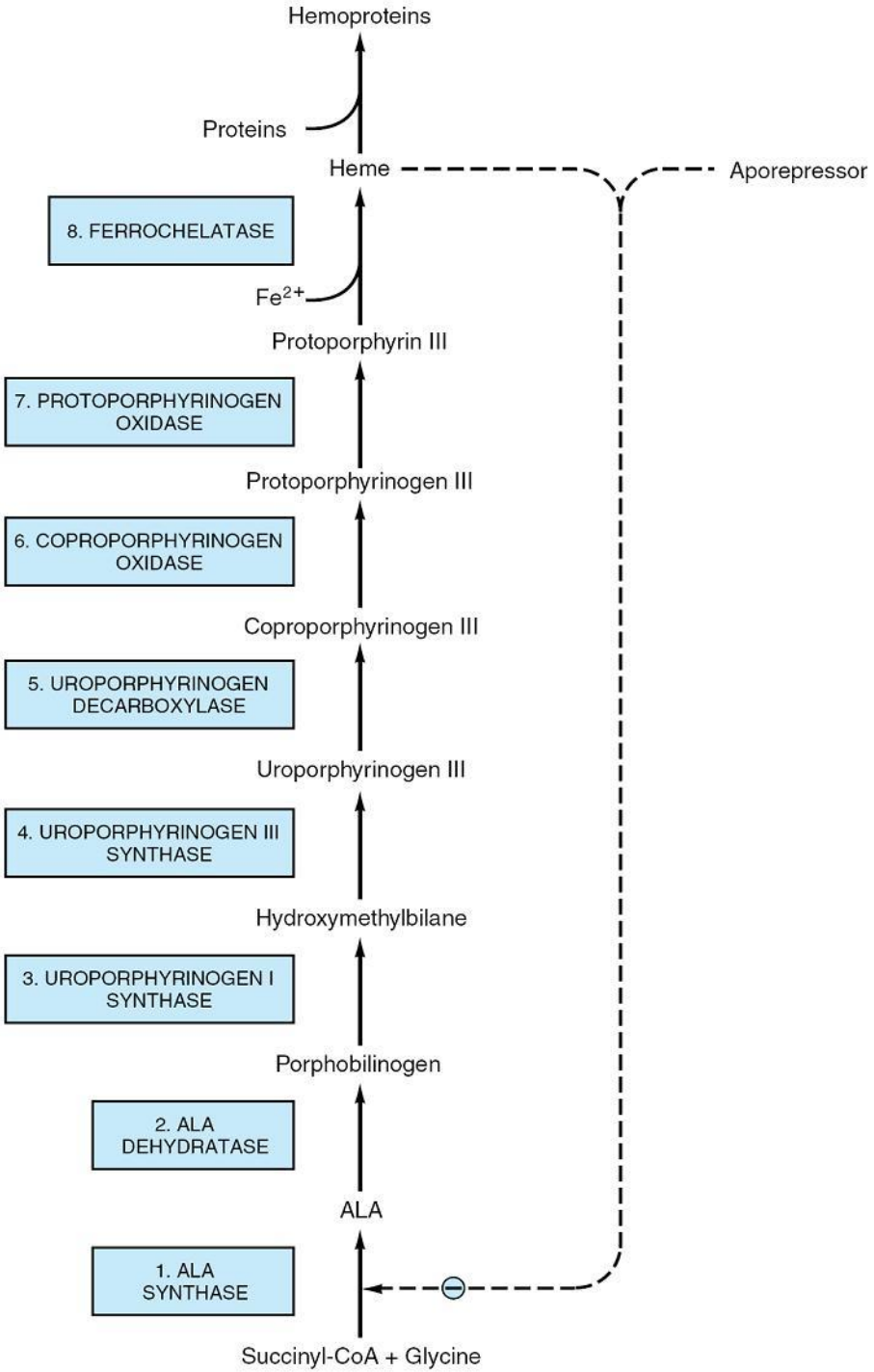
protoporphyrinogen IX

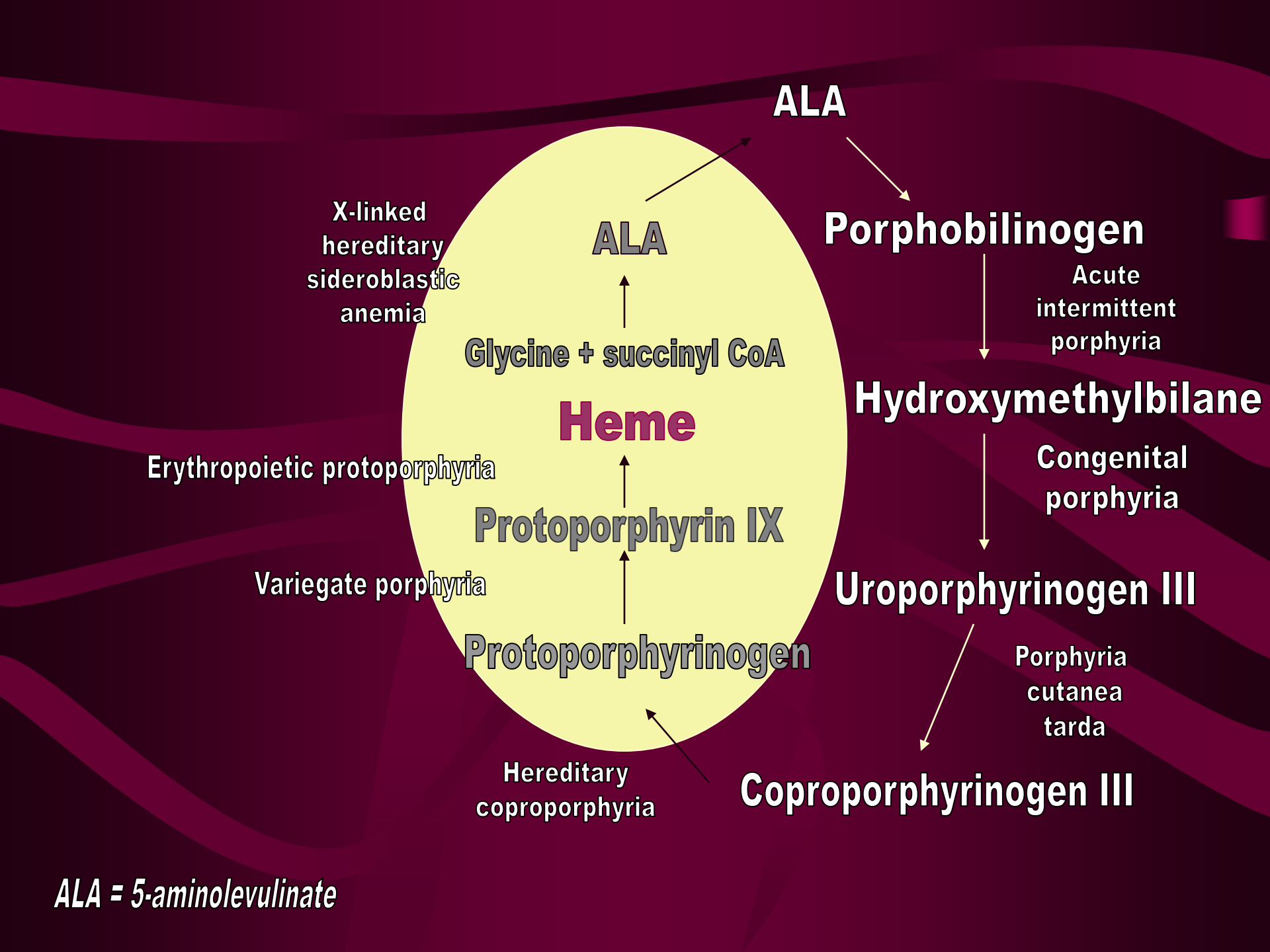

3/2O2
3 H2O
protoporphyrinogen III oxidase
protoporphyrinogen IX
protoporphyrin IX


Fe2+
2 H+
ferrochelatase
NH
N
H
H
N
HN
N
N
Fe2+
N
N
O
O
O
O
O
O
O
O
protoporphyrin IX
heme



ALA = 5-aminolevulinate


Hemoproteins
Proteins
Heme
Aporepressor
8. FERROCHELATASE
Fe2+
Protoporphyrin III
7. PROTOPORPHYRINOGEN OXIDASE
Protoporphyrinogen III
6. COPROPORPHYRINOGEN OXIDASE
Coproporphyrinogen III
5. UROPORPHYRINOGEN DECARBOXYLASE
Uroporphyrinogen III
4. UROPORPHYRINOGEN III SYNTHASE
Hydroxymethylbilane
3. UROPORPHYRINOGEN I SYNTHASE
Porphobilinogen
2. ALA DEHYDRATASE
ALA
1. ALA SYNTHASE
Succinyl-CoA + Glycine



ALA = 5-aminolevulinate

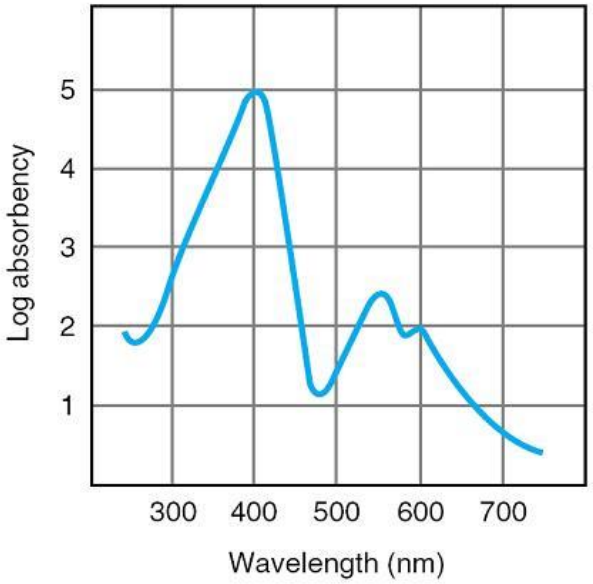
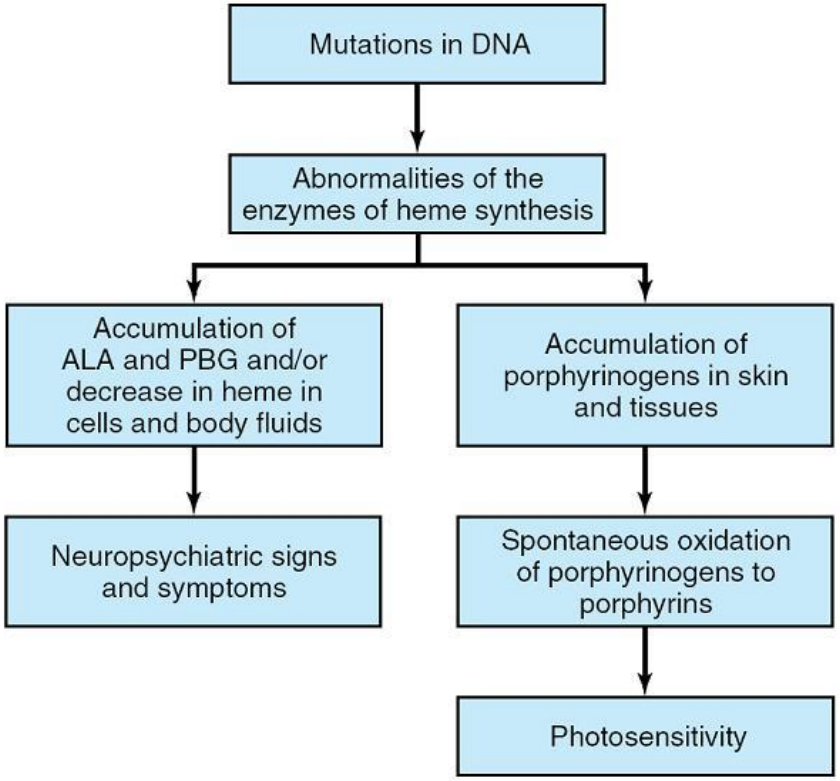


Figure 32–10. Absorption spectrum of hematoporphyrin (0.01% solution in 5% HCl).



Overview of Porphyrias:

- Classified into acute and non-acute
- Acute:
  - Acute intermittent porphyria
  - Variegate porphyria
  - Hereditary coproporphyria
- Non-acute:
  - Porphyria cutanea tarda
  - Erythropoietic protoporphyria
  - Congenital Porphyria

Porphyrinurias: lead, alcohol, iron-deficiency anemia, liver disease

Overview of Porphyrias:

- Each type is caused by absence or deficiency of an enzyme in the heme biosynthetic pathway
- Leads to increase in amount and excretion of heme precursors (in the case of acute porphyrias) or porphyrins (in the case of non-acute porphyrias)

Erythropoietic Protoporphyria

Porphyria Cutanea Tarda